

CLAIMS

We claim the following:

1 1. A method of stimulating the production of hematopoietic
2 cells in a patient comprising the step of administering a
3 polypeptide to the patient wherein the polypeptide is a human
4 flt-3 receptor agonist polypeptide comprising a modified flt-3
5 ligand amino acid sequence selected from the group consisting of:

6 (i) the sequence of SEQ ID NO: 144; and

7 (ii) a polypeptide comprising residues 1-132 of SEQ ID
8 NO:144;

9 wherein the modification comprises the linear rearrangement of
10 the sequences of (i) or (ii); wherein the N-terminus is joined to
11 the C-terminus directly or through a linker capable of joining
12 the N-terminus to the C-terminus and new C- and N-termini are
13 created between the amino acid residue pairs of SEQ ID NO:144
14 selected from the group consisting of:

15 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

16 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

17 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

18 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

19 and 102-103; and

20 wherein optionally the flt-3 receptor agonist polypeptide is
21 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
22 (methionine⁻², alanine⁻¹).

1 2. A method of stimulating the production of hematopoietic
2 cells in a patient comprising the step of administering a
3 composition to the patient wherein the composition comprises a
4 pharmaceutically acceptable carrier and a human flt-3 receptor
5 agonist polypeptide comprising a modified flt-3 ligand amino acid
6 sequence selected from the group consisting of:

7 (i) the sequence of SEQ ID NO: 144; and

8 (ii) a polypeptide comprising residues 1-132 of SEQ ID
9 NO:144;

10 wherein the modification comprises the linear rearrangement of
11 the sequences of (i) or (ii); wherein the N-terminus is joined to
12 the C-terminus directly or through a linker capable of joining
13 the N-terminus to the C-terminus and new C- and N-termini are
14 created between the amino acid residue pairs of SEQ ID NO:144
15 selected from the group consisting of:

16 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

17 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

18 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

19 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

20 and 102-103; and

21 wherein optionally the flt-3 receptor agonist polypeptide is
22 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
23 (methionine⁻², alanine⁻¹).

1 3. A method for selective ex vivo expansion of stem
2 cells comprising the steps of:

3 (a) separating hematopoietic cells from other cells;

4 (b) culturing the separated hematopoietic cells in a
5 culture medium comprising a human flt-3 receptor agonist
6 polypeptide comprising a modified flt-3 ligand amino acid
7 sequence selected from the group consisting of:

8 (i) the sequence of SEQ ID NO: 144; and

9 (ii) a polypeptide comprising residues 1-132 of SEQ ID
10 NO:144;

11 wherein the modification comprises the linear rearrangement of
12 the sequences of (i) or (ii); wherein the N-terminus is joined to
13 the C-terminus directly or through a linker capable of joining
14 the N-terminus to the C-terminus and new C- and N-termini are
15 created between the amino acid residue pairs of SEQ ID NO:144
16 selected from the group consisting of:

17 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

18 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

19 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

20 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

21 and 102-103; and

22 wherein optionally the flt-3 receptor agonist polypeptide is
23 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
24 (methionine⁻², alanine⁻¹); and
25 (c) harvesting the cultured cells.

1 4. A method for selective ex vivo expansion of
2 hematopoietic cells comprising the steps of:

3 (a) culturing the hematopoietic cells in a culture medium
4 comprising a composition including a pharmaceutically acceptable
5 carrier and a human flt-3 receptor agonist polypeptide comprising
6 a modified flt-3 ligand amino acid sequence selected from the
7 group consisting of:

8 (i) the sequence of SEQ ID NO: 144; and

9 (ii) a polypeptide comprising the residues 1-132 of SEQ
10 ID NO:144;

11 wherein the modification comprises the linear rearrangement of
12 the sequences of (i) or (ii); wherein the N-terminus is joined to
13 the C-terminus directly or through a linker capable of joining
14 the N-terminus to the C-terminus and new C- and N-termini are
15 created between the amino acid residue pairs of SEQ ID NO:144
16 selected from the group consisting of:

17 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,
18 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,
19 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,
20 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,
21 and 102-103; and

22 wherein optionally the flt-3 receptor agonist polypeptide is
23 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
24 (methionine⁻², alanine⁻¹); and
25 (b) harvesting the cultured cells.

1 5. A method for selective ex vivo expansion of
2 hematopoietic cells comprising the steps of:

3 (a) separating hematopoietic cells from other cells;

4 (b) culturing the separated hematopoietic cells in a
5 culture medium comprising a composition including a
6 pharmaceutically acceptable carrier and a human flt-3 receptor
7 agonist polypeptide comprising a modified flt-3 ligand amino acid
8 sequence selected from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and

10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

18 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

22 and 102-103; and

23 wherein optionally the flt-3 receptor agonist polypeptide is
24 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
25 (methionine⁻², alanine⁻¹); and
26 (c) harvesting the cultured cells.

1 6. A method for treatment of a patient having a
2 hematopoietic disorder comprising the steps of:

3 (a) removing hematopoietic cells from the patient;

4 (b) culturing the separated hematopoietic cells in a
5 culture medium comprising a human flt-3 receptor agonist
6 polypeptide comprising a modified flt-3 ligand amino acid
7 sequence selected from the group consisting of:

8 (i) the sequence of SEQ ID NO: 144; and

9 (ii) a polypeptide comprising residues 1-132 of SEQ ID
10 NO:144;

11 wherein the modification comprises the linear rearrangement of
12 the sequences of (i) or (ii); wherein the N-terminus is joined to
13 the C-terminus directly or through a linker capable of joining
14 the N-terminus to the C-terminus and new C- and N-termini are
15 created between the amino acid residue pairs of SEQ ID NO:144
16 selected from the group consisting of:

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19 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,
20 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,
21 and 102-103; and

22 wherein optionally the *flt-3* receptor agonist polypeptide is
23 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
24 (methionine⁻², alanine⁻¹);

25 (c) harvesting the cultured cells; and

26 (d) transplanting the cultured cells into the patient.

1 7. A method for treatment of a patient having a
2 hematopoietic disorder comprising the steps of:

3 (a) removing hematopoietic cells from the patient;

4 (b) separating the hematopoietic cells from other cells;

5 (c) culturing the separated hematopoietic cells in a
6 culture medium comprising a human flt-3 receptor agonist
7 polypeptide comprising a modified flt-3 ligand amino acid
8 sequence selected from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and

10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

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19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

22 and 102-103; and

23 wherein optionally the *flt-3* receptor agonist polypeptide is
24 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
25 (methionine⁻², alanine⁻¹);

26 (d) harvesting the cultured cells; and

27 (e) transplanting the cultured cells into the patient.

1 8. A method for treatment of a patient having a
2 hematopoietic disorder, comprising the steps of:

3 (a) removing hematopoietic cells from the patient;

4 (b) culturing the hematopoietic cells in a growth medium
5 comprising a human flt-3 receptor agonist polypeptide comprising
6 a modified flt-3 ligand amino acid sequence selected from the
7 group consisting of:

8 (i) the sequence of SEQ ID NO: 144; and

9 (ii) a polypeptide comprising residues 1-132 of SEQ ID
10 NO:144;

11 wherein the modification comprises the linear rearrangement of
12 the sequences of (i) or (ii); wherein the N-terminus is joined to
13 the C-terminus directly or through a linker capable of joining
14 the N-terminus to the C-terminus and new C- and N-termini are
15 created between the amino acid residue pairs of SEQ ID NO:144
16 selected from the group consisting of:

17 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

18 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

19 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

20 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

21 and 102-103; and

22 wherein optionally the flt-3 receptor agonist polypeptide is
23 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
24 (methionine⁻², alanine⁻¹);

25 (c) harvesting the cultured cells; and

26 (d) transplanting the cultured cells into the patient.

1 9. A method for treatment of a patient having a
2 hematopoietic disorder, comprising the steps of:

3 (a) removing hematopoietic cells from the patient;

4 (b) separating hematopoietic cells from other cells;

5 (c) culturing the separated hematopoietic cells in a growth
6 medium comprising a composition including a pharmaceutically
7 acceptable carrier and a human flt-3 receptor agonist polypeptide
8 comprising a modified flt-3 ligand amino acid sequence selected
9 from the group consisting of:

10 (i) the sequence of SEQ ID NO: 144; and

11 (ii) a polypeptide comprising residues 1-132 of SEQ ID
12 NO:144;

13 wherein the modification comprises the linear rearrangement of
14 the sequences of (i) or (ii); wherein the N-terminus is joined to
15 the C-terminus directly or through a linker capable of joining
16 the N-terminus to the C-terminus and new C- and N-termini are
17 created between the amino acid residue pairs of SEQ ID NO:144
18 selected from the group consisting of:

19 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

20 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

21 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

22 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

23 and 102-103; and

24 wherein optionally the flt-3 receptor agonist polypeptide is
25 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
26 (methionine⁻², alanine⁻¹);

27 (d) harvesting the cultured cells; and

28 (e) transplanting the cultured cells into the patient.

1 10. A method of human gene therapy comprising the steps
2 of:

3 (a) removing hematopoietic cells from a patient;

4 (b) culturing the hematopoietic cells in a growth medium
5 comprising a human flt-3 receptor agonist polypeptide comprising
6 a modified flt-3 ligand amino acid sequence selected from the
7 group consisting of:

8 (i) the sequence of SEQ ID NO: 144; and

9 (ii) a polypeptide comprising residues 1-132 of SEQ ID
10 NO:144;

11 wherein the modification comprises the linear rearrangement of
12 the sequences of (i) or (ii); wherein the N-terminus is joined to
13 the C-terminus directly or through a linker capable of joining
14 the N-terminus to the C-terminus and new C- and N-termini are
15 created between the amino acid residue pairs of SEQ ID NO:144
16 selected from the group consisting of:

17 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

18 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

19 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

20 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

21 and 102-103; and

22 wherein optionally the flt-3 receptor agonist polypeptide is
23 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
24 (methionine⁻², alanine⁻¹);

25 (c) transducing the cultured cells with DNA;

26 (d) harvesting the transduced cells; and

27 (e) transplanting the transduced cells into the patient.

1 11. A method of human gene therapy comprising the steps
2 of:

3 (a) removing hematopoietic cells from a patient;
4 (b) separating the hematopoietic cells from other cells;
5 (c) culturing the separated hematopoietic cells in a growth
6 medium comprising a human flt-3 receptor agonist polypeptide
7 comprising a modified flt-3 ligand amino acid sequence selected
8 from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and
10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

18 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,
19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,
20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,
21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,
22 and 102-103; and

1 wherein optionally the flt-3 receptor agonist polypeptide is
2 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
3 (methionine⁻², alanine⁻¹);

4 (d) transducing the cultured cells with DNA;

5 (e) harvesting the transduced cells; and

6 (f) transplanting the transduced cells into the patient.

1 12. A method of human gene therapy comprising the steps
2 of:

3 (a) removing hematopoietic cells from a patient;
4 (b) separating the hematopoietic cells from other cells;
5 (c) culturing the separated hematopoietic cells in a growth
6 medium comprising a composition including a pharmaceutically
7 acceptable carrier and a human flt-3 receptor agonist polypeptide
8 comprising a modified flt-3 ligand amino acid sequence selected
9 from the group consisting of:

10 (i) the sequence of SEQ ID NO: 144; and
11 (ii) a polypeptide comprising residues 1-132 of SEQ ID
12 NO:144;

13 wherein the modification comprises the linear rearrangement of
14 the sequences of (i) or (ii); wherein the N-terminus is joined to
15 the C-terminus directly or through a linker capable of joining
16 the N-terminus to the C-terminus and new C- and N-termini are
17 created between the amino acid residue pairs of SEQ ID NO:144
18 selected from the group consisting of:

19 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,
20 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,
21 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,
22 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,
23 and 102-103; and

24 wherein optionally the flt-3 receptor agonist polypeptide is
25 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
26 (methionine⁻², alanine⁻¹);

27 (d) transducing the cultured cells with DNA;

28 (e) harvesting the transduced cells; and

29 (f) transplanting the transduced cells into the patient.

1 13. A method of human gene therapy comprising the steps
2 of:

3 (a) removing hematopoietic cells from a patient;
4 (b) separating the hematopoietic cells from other cells;
5 (c) culturing the separated hematopoietic cells in a growth
6 medium comprising a composition including a pharmaceutically
7 acceptable carrier and a human flt-3 receptor agonist polypeptide
8 comprising a modified flt-3 ligand amino acid sequence selected
9 from the group consisting of:

10 (i) the sequence of SEQ ID NO: 144; and
11 (ii) a polypeptide comprising residues 1-132 of SEQ ID
12 NO:144;

13 wherein the modification comprises the linear rearrangement of
14 the sequences of (i) or (ii); wherein the N-terminus is joined to
15 the C-terminus directly or through a linker capable of joining
16 the N-terminus to the C-terminus and new C- and N-termini are
17 created between the amino acid residue pairs of SEQ ID NO:144
18 selected from the group consisting of:

19 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,
20 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,
21 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,
22 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,
23 and 102-103; and

24 wherein optionally the *flt-3* receptor agonist polypeptide is
25 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
26 (methionine⁻², alanine⁻¹);

27 (d) transducing the cultured cells with DNA;

28 (e) harvesting the transduced cells; and

29 (f) transplanting the transduced cells into the patient.

1 14. A method for the production of dendritic cells
2 comprising the steps of:

3 (a) separating hematopoietic progenitor cells or CD34+
4 cells from other cells; and

5 (b) culturing the hematopoietic progenitor cells or CD34+
6 cells in a growth medium comprising a human flt-3 receptor
7 agonist polypeptide comprising a modified flt-3 ligand amino acid
8 sequence selected from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and

10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

18 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

22 and 102-103; and

23 wherein optionally the flt-3 receptor agonist polypeptide is
24 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
25 (methionine⁻², alanine⁻¹).

1 15. The method of claim 14 further comprising the step of
2 pulsing the culturing hematopoietic progenitor cells or CD34+
3 cells with an antigen.

1 16. The method of claim 14 wherein the growth medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 17. The method of claim 15 wherein the growth medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 18. A method for treating a human having a tumor, infection
2 or auto-immune disease comprising the step of administering a
3 human flt-3 receptor agonist polypeptide comprising a modified
4 flt-3 ligand amino acid sequence selected from the group
5 consisting of:

6 (i) the sequence of SEQ ID NO: 144; and

7 (ii) a polypeptide comprising residues 1-132 of SEQ ID
8 NO:144;

9 wherein the modification comprises the linear rearrangement of
10 the sequences of (i) or (ii); wherein the N-terminus is joined to
11 the C-terminus directly or through a linker capable of joining
12 the N-terminus to the C-terminus and new C- and N-termini are
13 created between the amino acid residue pairs of SEQ ID NO:144
14 selected from the group consisting of:

15 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

16 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

17 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

18 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

19 and 102-103; and

20 wherein optionally the flt-3 receptor agonist polypeptide is
21 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
22 (methionine⁻², alanine⁻¹) to the human.

1 19. The method of claim 18 further comprising
2 administering one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 20. The method of claim 18 further comprising the step of
2 administering an antigen to the patient.

1 21. The method of claim 19 further comprising the step of
2 administering an antigen to the patient.

22. A method for treating a human having a tumor, infection or auto-immune disease, comprising the steps of:

(a) mobilizing dendritic cell progenitors or mature dendritic cells by administering a human flt-3 receptor agonist polypeptide comprising a modified flt-3 ligand amino acid sequence selected from the group consisting of:

(i) the sequence of SEQ ID NO: 144; and

(ii) a polypeptide comprising residues 1-132 of SEQ ID NO:144;

wherein the modification comprises the linear rearrangement of the sequences of (i) or (ii); wherein the N-terminus is joined to the C-terminus directly or through a linker capable of joining the N-terminus to the C-terminus and new C- and N-termini are created between the amino acid residue pairs of SEQ ID NO:144 selected from the group consisting of:

28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

and 102-103; and

wherein optionally the flt-3 receptor agonist polypeptide is immediately preceded by (methionine⁻¹), (alanine⁻¹) or (methionine⁻², alanine⁻¹) to the human;

24 (b) removing the dendritic cell precursors or mature
25 dendritic cells by a blood draw or pheresis;
26 (c) pulsing the dendritic cell precursors or mature
27 dendritic cells with an antigen; and
28 (d) returning the antigen pulsed dendritic cell precursors
29 or mature dendritic cells to the human.

1 23. The method of claim 22 further comprising administering
2 in step (a) one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 24. The method of claim 22 further comprising the step of
2 culturing said dendritic cell precursors or mature dendritic
3 cells from step (b) in a growth medium comprising the human flt-3
4 receptor agonist polypeptide.

1 25. The method of claim 23 further comprising the step of
2 culturing the dendritic cell precursors or mature dendritic cells
3 from step (b) in a growth medium comprising the human flt-3
4 receptor agonist polypeptide.

1 26. The method of claim 24 wherein the growth medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 27. The method of claim 25 wherein the growth medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 28. A method for treating a human having a tumor, infection
2 or auto-immune disease comprising the steps of:

3 (a) removing hematopoietic progenitor cells or CD34+ cells
4 from the human by a blood draw or pheresis;

5 (b) culturing the hematopoietic progenitor cells or CD34+
6 cells in a growth medium comprising a human flt-3 receptor
7 agonist polypeptide comprising a modified flt-3 ligand amino acid
8 sequence selected from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and

10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

18 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

22 and 102-103; and

23 wherein optionally the flt-3 receptor agonist polypeptide is
24 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
25 (methionine⁻², alanine⁻¹) to produce dendritic cell precursors or
26 mature dendritic cells; and

27 (c) returning the dendritic cell precursors or mature
28 dendritic cells to the human.

1 29. A method for treating a human having a tumor, infection
2 or auto-immune disease comprising the steps of:

3 (a) removing hematopoietic progenitor cells or CD34+ cells
4 from the patient by a blood draw or pheresis;

5 (b) culturing the hematopoietic progenitor cells or CD34+
6 cells in a growth medium comprising a human flt-3 receptor
7 agonist polypeptide comprising a modified flt-3 ligand amino acid
8 sequence selected from the group consisting of:

9 (i) the sequence of SEQ ID NO: 144; and

10 (ii) a polypeptide comprising residues 1-132 of SEQ ID
11 NO:144;

12 wherein the modification comprises the linear rearrangement of
13 the sequences of (i) or (ii); wherein the N-terminus is joined to
14 the C-terminus directly or through a linker capable of joining
15 the N-terminus to the C-terminus and new C- and N-termini are
16 created between the amino acid residue pairs of SEQ ID NO:144
17 selected from the group consisting of:

18 28-29, 29-30, 30-31, 31-32, 32-33, 34-35, 36-37, 37-38,

19 38-39, 40-41, 41-42, 42-43, 64-65, 65-66, 66-67, 86-87,

20 87-88, 88-89, 89-90, 90-91, 91-92, 92-93, 93-94, 94-95,

21 95-96, 96-97, 97-98, 98-99, 99-100, 100-101, 101-102,

22 and 102-103; and

23 wherein optionally the flt-3 receptor agonist polypeptide is
24 immediately preceded by (methionine⁻¹), (alanine⁻¹) or
25 (methionine⁻², alanine⁻¹) to produce dendritic cell precursors or
26 mature dendritic cells;

27 (c) pulsing the dendritic cell precursors or mature
28 dendritic cells with an antigen; and

29 (d) returning the antigen pulsed dendritic cell precursors
30 or mature dendritic cells to the human.

1 30. The method of claim 28 further comprising the step of
2 separating the hematopoietic progenitor cells or CD34+ cells from
3 other cells prior to culturing.

1 31. The method of claim 29 further comprising the step of
2 separating the hematopoietic progenitor cells or CD34+ cells from
3 other cells prior to culturing.

1 32. The method of claim 28 wherein the culture medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 33. The method of claim 29 wherein the culture medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 34. The method of claim 30 wherein the culture medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.

1 35. The method of claim 31 wherein the culture medium
2 further comprises one or more factors selected from the group
3 consisting of: GM-CSF, IL-4, TNF- α , stem cell factor (SCF), flt-
4 3 ligand, IL-3, an IL-3 variant, an IL-3 variant fusion protein,
5 and a multi-functional receptor agonist.